

**REMARKS**

This amendment is responsive to the Office Action mailed October 8, 2003. Rather than substantially amend the existing claim set, Applicant has cancelled Claims 1-45 herein and submits new Claims 46-71. The claims have been amended to more particularly point out and distinctly claim the particularly inventive embodiments of the present invention. Specifically, Applicant has focused the claims to methods of preserving viruses, bacteria or other viable cells using preservation mixtures comprising a methylated monosaccharide, such as  $\alpha$ -methyl glucose and  $\beta$ -methyl glucose (*See*, page 3, lines 1-3), and a disaccharide or oligosaccharide.

The following chart illustrates the support for each new claim with reference to an original claim or claims, or to particular passages of the specification.

| New Claim number<br>(introduced herein) | Former Claim<br>Number(s) | Specification Support<br>(U.S. Appln. Serial No. 09/721,609) |
|---|---------------------------|--|
| 46                                      | 1, 2, 5, and 6            |  |
| 47                                      | 3                         |  |
| 48                                      | 4                         |  |
| 49                                      | 15                        |  |
| 50                                      | 16                        |  |
| 51                                      | 17                        |  |
| 52                                      | 18                        |  |
| 53                                      | 21 and 6                  |  |
| 54                                      |                           | pg. 1, lines 15-18; pg. 5, lines 4-27                        |
| 55                                      | 24, 26, and 27            |  |
| 56                                      | 25, 26, and 27            |  |
| 57                                      | 28                        |  |
| 58                                      | 36                        |  |
| 59                                      | 37                        |  |
| 60                                      | 38                        |  |
| 61                                      | 39                        |  |
| 62                                      | 42                        |  |
| 63                                      | 44                        |  |
| 64                                      | 45                        |  |
| 65                                      |                           | pg. 12, lines 1-10   |
| 66                                      |                           | pg. 13, lines 6-11   |
| 67                                      |                           | pg. 13, lines 6-11   |
| 68                                      |                           | pg. 10, lines 10-22  |
| 69                                      |                           | pg. 10, lines 10-22  |
| 70                                      | 1, 2, 5 and 6             | pg. 2, lines 10-14   |
| 71                                      |                           | pg. 13, lines 6-11   |

No new matter is presented by the introduction of Claims 46-71.

**Response to issues presented under 35 U.S.C. §102**

Original Claims 1-4, 20-25, 28, 41, and 44-45 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by U.S. Patent No. 5,766,520 to Bronshtein (hereinafter "the '520 patent").

A rejection for anticipation under 35 U.S.C. §102 requires that each and every limitation of the claimed invention be disclosed in a single prior art reference. *See* MPEP §2131. Whereas the reference of record fails to disclose or suggest aspects of the invention that are particularly and distinctly claimed, reconsideration and withdrawal of the rejection under 35 U.S.C. §102 are requested.

The '520 patent teaches the preservation of sensitive biological samples by the formation of stable foams. The foams are formed by partially dehydrating the fluid sample to form a viscous liquid. The viscous liquid is then further dried by boiling the sample under a vacuum, resulting in a boiling point substantially lower than 100° C. The boiling causes the viscous solution to "foam", which maximizes the liquid surface area for evaporation, and results in a dry foam product that is easily divisible by cutting, milling, etc. The application mentions in passing that this drying process may incorporate vitrifying enhancers and other protectants, such as: "sugars (including sucrose among others), carbohydrates, polysaccharides, water-soluble polymers, peptides or proteins as long as the protectant enhances the ability of the biologically active material to withstand drying and storage and does not interfere with the particular biological activity." (Column 2, line 66 - Column 3, line 5.) The application also mentions that the foams may be subjected to subsequent secondary drying. Both examples in the patent incorporated a 50% by weight sucrose solution.

The novelty of the present invention, on the other hand, involves the discovery that non-reducing derivatives of monosaccharides, such as methyl- $\alpha$ -D-glucopyranoside, are particularly well suited for the preservation of cells and viruses, most likely due to interactions between the methyl group and hydrophobic regions of proteins, virus envelopes and other membrane structures. *See, e.g.*, page 9, lines 19-30 of the specification. As Applicant's data proves, methyl- $\alpha$ -D-glucopyranoside surprisingly exhibits superior protective qualities in comparison with non-methylated monosaccharides. *See, e.g.*, Examples 1-3 of the specification. Moreover, the combination of a methylated monosaccharide and a disaccharide as a preservation mixture for viruses or bacteria is surprisingly superior to other types of mixtures. *See, e.g.*, Examples 6-9.

Particularly, Applicant's data shows virus preservation mixtures comprising a 2:1 sucrose:methyl- $\alpha$ -D-glucopyranoside ratio exhibited consistent elevated virus survival rates when compared to other preservation mixtures. *See, e.g.*, Examples 6, 7, 9. Similarly, Applicant's data showed cell preservation mixtures comprising a 1:1 sucrose:methyl- $\alpha$ -D-glucopyranoside exhibited unsurpassed bacterial cell survival rates compared to the other preservation mixtures. *See, e.g.*, Example 8.

Applicant notes that the claims have been amended herein to more precisely reflect the novelty of the present invention over the prior art. Independent Claims 46 and 53 now recite:

46. (new) A preservation mixture comprising:  
a virus, bacteria, or other cell which is sensitive to loss of viability during drying and storage at ambient or higher temperatures;  
a methylated monosaccharide selected from the group consisting of methyl  $\alpha$ -glucopyranoside and methyl  $\beta$ -glucopyranoside; and  
a disaccharide selected from the group consisting of sucrose and trehalose, or, alternatively, an oligosaccharide.

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53. (new) A method of preserving a virus, bacteria or other cell which is sensitive to loss of viability during drying and storage at ambient or higher temperatures, the method comprising:  
mixing the virus, bacteria or other cell with a protectant comprising a methylated monosaccharide selected from the group consisting of methyl ( $\alpha$  or  $\beta$ )-glucose and at least one additional compound selected from the group consisting of disaccharides and oligosaccharides to form a preservation mixture; and  
drying the preservation mixture by foam formation comprising the formation of a mechanically stable porous foam structure by boiling said preservation mixture under a vacuum.

Applicant contends that the amended claims of the present invention are not anticipated by the '520 patent. Applicant's specification teaches novel, inventive preservation mixtures, which were surprisingly shown to be more effective than traditional preservation mixtures suggested by the prior art. Moreover, as Applicant discloses, the preservation mixtures of the present invention may be utilized in a variety of drying protocols, including but not limited to vitrification.

Therefore, because the '520 patent fails to teach or suggest aspects of the invention as particularly and distinctly set forth in the claims, Applicant requests reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b).

**Response to issues presented under the judicially-created doctrine of  
obviousness-type double patenting**

**U.S. Patent No. 6,509,146**

In the Office Action, Claims 1-45 were rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 1-6 of U.S. Patent No. 6,509,146 (hereinafter "the '146 patent"). Specifically, the Examiner contends that although the claims are not identical, they are not patentably distinct because they are of the same inventive concept, namely the preservation of a biological at ambient temperatures with a given protectant mixture.

Applicant traverses. The '146 patent is mainly directed to preserving biologicals through vitrification. The patent suggests that when cells and viruses are to be preserved, a composition comprising a low molecular weight sugar, a disaccharide, and a high molecular weight biological polymer can be used. (*See, e.g.* the paragraph bridging column 5 and 6.). The '146 patent teaches the inclusion of a low molecular weight sugar when preserving cells because they are able to penetrate and protect intracellular structures during dehydration. (Column 5, lines 61-63.) The patent also teaches the inclusion of disaccharides because they are known to replace the water molecules on the surface of biological membranes during dehydration. Additionally, the '146 patent teaches that:

"[C]ombining a low molecular weight non-reducing sugar, like fructose, with disaccharides, like sucrose, effectively prevents crystallization of the disaccharide during dehydration." (Column 6, lines 14-17.)

In fact the only example in the '146 patent of preservation mixtures to preserve cells is Example 8, which teaches the preservation of *E. coli* cells in a preservation solution consisting of 25% sucrose and 25% fructose in MRS broth.

As discussed above, the novelty of the present invention involves the discovery that non-reducing derivatives of monosaccharides, such as methyl- $\alpha$ -D-glucopyranoside, are particularly well suited for the preservation of cells and viruses, most likely due to interactions between the methyl group and hydrophobic regions of proteins, virus envelopes and other membrane structures. *See, e.g.*, page 9, lines 19-30 of the specification. As shown by the Applicant in *this* application, methyl- $\alpha$ -D-glucopyranoside surprisingly exhibits superior protective qualities in comparison with non-methylated monosaccharides. *See, e.g.*, Examples 1-3 of the specification, and the combination of a methylated monosaccharide and a

disaccharide (without additional protectants) as a preservation mixture for viruses or bacteria is surprisingly superior to other types of mixtures. *See, e.g.*, Examples 6-9.

As the CAFC has stated regarding obvious-type double patenting:

"Under that facet of the doctrine of double patenting, we must direct our inquiry to whether the claimed invention in the application for the second patent would have been obvious from the subject matter of the claims in the first patent, in light of the prior art." *In re Longi*, 225 USPQ 645, 648 (Fed. Cir. 1985) (citing *Carman Industries Inc. v. Wahl*, 220 USPQ 481, 487 (Fed. Cir. 1983)). (Emphasis added.)

Applicant submits that his amended claims to directed preservation mixtures comprising non-reducing derivatives of monosaccharides, such as methyl- $\alpha$ -D-glucopyranoside and a disaccharide are not obvious over the '146 patent, because the preservation mixtures of the present application have been shown to possess unexpected results, i.e., the unexpectedly surprising superiority in preserving cells and viruses. The superiority of preservation mixtures containing methylated monosaccharides and a disaccharide is not disclosed, or even suggested, in the '146 patent.

The courts have made it clear that unexpected scientific data that demonstrates an improvement over the disclosure of the closest prior art is an important indicator of non-obviousness, i.e., it is sufficient to overcome even a *prima facie* case of obviousness. For example, in *In re Soni*, 54 F.3d 746, 34 USPQ2d 1684 (Fed. Cir. 1995), the applicant, Soni, claimed a composition comprising an organic polymer with a molecular weight greater than 150,000 and a particulate conductive filler. Additionally, the applicant claimed that the composition demonstrated unexpected and significant improvements over the properties of compositions of the prior art, which utilized organic polymers with molecular weights less than 150,000. Soni also included test data comparing the properties of the claimed invention, i.e., organic polymers with molecular weight greater than 150,000, with those of the prior art, i.e., organic polymers with a molecular weight less than 150,000. The examiner and the PTO Board of Appeals dismissed the applicant's data, essentially stating that one skilled in the art would expect higher molecular weight polymers to result in better composition properties and further stating that the unexpected results consisted of conclusory statements unsupported by any factual data.

Soni appealed to the Federal Circuit, where the issue was whether the data in Soni's patent specification showed that the claimed compositions demonstrated "unexpectedly improved" properties compared to the prior art lower molecular weight compositions. According to the Court,

"One way for a patent applicant to rebut a *prima facie* case of obviousness is to make a showing of "unexpected results", i.e., to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected." 54 F.3d at 750, 34 USPQ2d at 1687 (Emphasis added.)

Additionally the Court stated,

"The principle applies most often to the less predictable fields, such as chemistry, where minor changes in a product or a process may yield substantially different results." 54 F.3d at 750, 34 USPQ2d at 1687 (Emphasis added.)

After analyzing the data in Soni's application, the Court overturned the Board's holding, stating, "In our view, however, when an applicant demonstrates *substantially* improved results, as Soni did here, and *states* that the results were *unexpected*, this should suffice to establish unexpected results *in the absence of* evidence to the contrary." 54 F.3d at 751, 34 USPQ2d at 1688. (Emphasis in original.)

As illustrated by the data in *this* application, methyl- $\alpha$ -D-glucopyranoside surprisingly exhibits superior protective qualities in comparison with non-methylated monosaccharides. *See, e.g.*, Examples 1-3 of the specification, and the combination of a methylated monosaccharide and a disaccharide (without additional protectants) as a preservation mixture for viruses or bacteria is surprisingly superior to other types of mixtures, Examples 6-9.

Therefore, since the compounds and methods of the present invention possess advantageous and unexpected properties that could not have been perceived or imagined by those skilled in the art from consideration of the '146 patent, Applicant requests reconsideration of the rejection under the judicially created doctrine of obvious-type double patenting and acknowledgment that new Claims 46-71 herein are not subject to such doctrine.

#### U.S. Patent No. 6,306,345

In the Office Action, Claims 1-45 also were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over Claims 1-11 of U.S. Patent No. 6,306,345 (hereinafter "the '345 patent"). Again, the Examiner contends that although the claims are not identical, they are not patentably distinct because they are of the same inventive concept, namely the preservation of a biological at ambient temperatures with a given protectant mixture.

Applicant respectfully traverses. The '345 patent discloses and claims a barrier method of drying, wherein the drying takes place in isolated deformable (semi-rigid) containers to aid in the subsequent crushing of the brittle foam into a powder. (*See*, Examples 1-4 in Columns 13-14.) Such drying processes, while useful, are irrelevant to the present invention directed to preservation mixtures containing methylated monosaccharides and a disaccharide.

While the '345 patent suggests that when cells and viruses are to be preserved, a composition comprising a low molecular weight sugar, a disaccharide, and a high molecular weight biological polymer can be used (*see*, e.g., the paragraph bridging column 4 and 5), Applicant notes that this disclosure is a verbatim repetition of the disclosure of the '146 patent, discussed above. Therefore, Applicant submits that his amended claims are non-obvious over the '345 patent for the reasons detailed above in distinguishing the '146 patent.

Accordingly, since the compounds and methods of the present invention possess advantageous and unexpected properties that could not have been perceived or imagined by those skilled in the art from consideration of the '345 patent, Applicant requests reconsideration and withdrawal of the rejection under the judicially created doctrine of obvious-type double patenting and acknowledgement that new Claims 16-71 are not subject to such doctrine.

In view of the amendments herein and the foregoing remarks, reconsideration and allowance of the claims as amended are respectfully requested.

Respectfully submitted,



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